REMARKS

Prior to entry of this Amendment, Claims 18, 20-27, 36 and 37 were pending and under consideration. Claim 26 has been withdrawn from consideration. With this Amendment, Claim 18 is being amended and Claims 36 and 37 are being cancelled, without prejudice against their reintroduction in this or one or more related applications. No claims are being added. Thus, after entry of this Amendment, Claims 18, and 20-27 are pending and under consideration. The amendments of the claims and the rejections raised in the Office Action are discussed in detail below.

Claim Amendments

Claim 18 and has been amended to recite "the voltage associated with". Support for amended Claim 18 is found in the specification at pages 72-3, lines 15-2, page 74, lines 16-25, and 74-5, lines 34-2. No new matter is added by the amendment of Claim 18. Accordingly, entry into the instant Application is proper and respectfully requested.

Claim Objection

Claim 37 is objected to under 37 C.F.R. 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim because Claim 36 has a detector and Claim 37 does not further limit the detector of Claim 36. The objection is moot in light of the cancellation of Claim 37.

Claim Rejection Under 35 USC §102(e)

Claims 18, 27, 36, and 37 are rejected under 35 U.S.C. §102(e) as allegedly being anticipated by *Heller et al.* (U.S. Patent No. 6,652,808), as evidenced by *Kayyem* (U.S. Patent No. 6,063,573). Applicants traverse the rejection with respect to Claims 18 and 27 and although Applicants disagree with the propriety of the rejection, in order to expedite prosecution of claims reciting methods of treatment, Applicants have canceled Claims 36 and 37, rendering the rejection moot.

Amended Claim 18 recites a composition comprising a substrate comprising an array of electrodes, wherein each electrode comprises a binding ligand, a plurality of colloids, each comprising a binding ligand partner, and an electron transfer moiety, and a detector capable of detecting the voltage associated with electron transfer from said electron transfer moiety. Claim 27 depends from Claim 18.

The Examiner asserts that *Heller* teaches a fluorescent dye on nanobeads is an electron transfer moiety. Office Action at page 3. Further, the Examiner assert that *Heller* teaches an avalanche photo diode array detector that can detect multiple fluorescent color response and *Kayyem* shows one way to detect electron transfer is fluorescence detection. As such the Examiner argues that *Heller* as evidenced by *Kayyem* teach a detector capable of detecting electronic transfer from an electron transfer moiety. Office Action at page 4.

For an anticipation rejection under 35 U.S.C. §102(e) to be proper, a single reference must expressly or inherently disclose each and every element of a claim. *In re Paulsen*, 31 USPQ2d 1671, 1673 (Fed. Cir. 1994); MPEP § 2131 (citing *Richardson v. Suzuki Motor Co.*, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989).

Without agreeing with the Examiner's position, Applicants respectfully assert that *Heller* does not teach the invention as defined in amended Claim 18 and dependent Claim 27. *Heller* teaches a photo diode array detector that can detect multiple fluorescent color responses. *Heller* does not disclose a composition comprising a substrate comprising an array of electrodes, wherein each electrode comprises a binding ligand, a plurality of colloids, each comprising a binding ligand partner, and an electron transfer moiety, and a detector capable of detecting the voltage associated with electron transfer from said electron transfer moiety as required by Claim 18 and dependent Claim 27. As such, *Heller* cannot anticipate Claims 18 and 27.

Kayyem cannot be used to supplement *Heller* in such a way as to show that *Heller* anticipates Claims 18 and 27. *Kayyem* does not disclose a composition comprising a substrate comprising an array of electrodes, wherein each electrode comprises a binding

ligand, a plurality of colloids, each comprising a binding ligand partner, and an electron transfer moiety, and a detector capable of detecting the voltage associated with electron transfer from said electron transfer moiety as required by Claim 18 and dependent Claim 27.

Accordingly, *Heller*, as evidence by *Kayyem* fails teach each and every limitation of the rejected Claims 18 and 27, and therefore cannot anticipated these claims. Thus, Applicants respectfully request withdrawal of the rejection. The rejection of Claims 36 and 37 is moot in light of cancellation of Claims 36 and 37.

Claim Rejection Under 35 USC §103(a)

Claims 20 and 21 are rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over *Heller et al.* (U.S. Patent No. 6,652,808), as evidenced by *Kayyem* (U.S. Patent No. 6,063,573), and further in view of *Sigal et al.* (U.S. Patent No. 6,319,670). The rejection is traversed with respect to Claims 20 and 21.

In rejecting claims under §103(a), the Patent Office bears the burden of establishing a *prima facie* case of obviousness (MPEP § 2142). To establish a *prima facie* case, three basic criteria must be met. First, the prior art reference(s) must teach or suggest each and every limitation of the rejected claims. Second, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the references or to combine their teachings. Third, there must be a reasonable expectation of success. The teaching or suggestion to make the claimed combination *and* the reasonable expectation of success must *both* be found in the prior art, and *not* in Applicants' disclosure. *In re Vaeck*, 20 USPQ2d 1438 (Fed. Cir. 1991); MPEP §2142.

Neither the *Heller* nor the *Kayyem* reference, alone or in combination, teach or suggest a composition comprising a substrate comprising an array of electrodes, wherein each electrode comprises a binding ligand, a plurality of colloids, each comprising a binding ligand partner, and an electron transfer moiety; and a detector capable of

detecting the voltage associated with electron transfer from said electron transfer moiety as required by Claim 18. Claims 20 and 21 depend ultimately from Claim 18.

The Examiner asserts *Sigal* teaches array ligands coating the particle to form a self assembled monolayer, *Sigal* disclose a plurality of colloids comprises a self-assembled monolayer as recited in Claim 20. Further the Examiner asserts that *Sigal* teaches array ligands can be amino acids and it is know in the art that some amino acids such as lysine have two or more CH_2 groups (alkyl groups), such that *Sigal* disclose that the self-assembling monolayer comprise an alkyl chain as recited in Claim 21. Office Action at page 5. *Sigal* fails teach or suggest a composition comprising a substrate comprising an array of electrodes, wherein each electrode comprises a binding ligand, a plurality of colloids, each comprising a binding ligand partner; and an electron transfer moiety, and a detector capable of detecting the voltage associated with electron transfer from said electron transfer moiety. In fact, the Examiner admits that *Signal* teaches electrochemiluminescent assay. Office Action at page 6. As the cited references alone, or in combination, do not teach or suggest all of the claim limitations, the Examiner has not established a *prima facie* case of obviousness, and therefore withdrawal of the instant rejection is respectfully requested.

Assuming *arguendo* that all of the elements of an invention are found in a combination of prior art references, a proper analysis under Section 103(a) requires consideration of two factors: (1) whether the prior art would have suggested to those of ordinary skill in the art that they should make the claimed composition or device, or carry out the claimed process; and (2) whether the prior art would also have revealed that in so making or carrying out, those of ordinary skill would have had a reasonable expectation of success. *Noelle v. Lederman*, 69 USPQ2d 1508, 1515 (Fed. Cir. 2004). In determining *prima facie* obviousness, the Patent Office must consider not only the cited references, but all evidence of record, MPEP § 2142.

As an initial matter the Examiner asserts, "it is known in the art that activation of a fluorescent dye includes electron transfer, and according to the definition of the

specification the fluorescent dye on the nanobeads or nanoparticles taught by *Heller* is an electron transfer moiety as recited in Claim 18. Office action at page 3. Applicants respectfully disagree. In *Edman*, Proc. Natl. Acad. Sci. Vol. 93, 6710-15 (1996), previously relied by the Examiner, *Edman* teaches that rhodamine quenching requires a guanosine rich area and only "guanosine quenches rhodamines profoundly, and no other nucleotide base will accomplish this". Abstract and page 671, second to last paragraph. Further, *Seidel* (J. Phys. Chem 11, 5541-5553 (1996)) previously relied by the Examiner, teaches that not all fluorescent dyes are capable of electron transfer from nucleotides. In fact, *Seidel* teaches that while fluorescent dye C-120 can be quenched by dC, dT, U, and P, the fluorescent dye C-307 remains unquenched by these nucleosides, and in the case nucleobase derivatives, quenching is unfavorable. *Seidel* at pages 5545 last paragraph, and at 5546 second full paragraph. Further, Applicants note that experimental oxidation potentials of the guanine, adenine, cytosine, thymine, and uracile range from 1.49 to greater than 2.39 volts. *See Seidel* at Table 2. On the contrary, the instant specification teaches that AC amplitude ranges from about 1 mV to about 1.1 volts. Thus, *Edman* and *Seidel* do not teach, as the Patent Office contends, it is known in the art that activation of a fluorescent dye includes electron transfer. In light of the preceding, the Examiner has failed to establish a motivation to combine the cited references. Accordingly, a *prima facie* case of obviousness based on those references has not been established and withdrawal of the rejection is respectfully requested.

Similarly, the remaining rejections (Claims 22, 23 24, and 25) rely on *Heller's* disclosure of fluorescent beads and particles as the teaching of electron transfer moieties. Accordingly, the Examiner has also failed to establish a prima facie case of obviousness in each of those cases, as the Examiner has not shown that the cited references teach or suggest, alone or in combination, each and every claim limitation. Therefore, withdrawal of each of those rejections is also respectfully requested. The rejection of Claims 36 and 37 under Section 103(a) are moot in light of cancellation of Claims 36 and 37.

CONCLUSION

Applicants respectfully submit that the claims are now in condition for allowance and early notification to that effect is respectfully requested. If the Examiner feels there are further unresolved issues, the Examiner is respectfully requested to phone the undersigned at (415) 781-1989.

Respectfully submitted,
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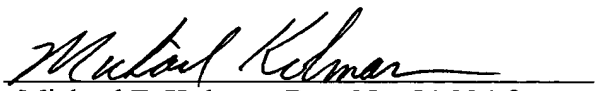
Dated: May 2, 2005 By: 
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